REMARKS

Claims 21-26 are pending in the present application. The Examiner has rejected these Claims in an Office Action mailed June 17, 2003. For clarity, the rejections at issue are set forth by number in the order they are addressed herein:

(1) Claims 21-32 are indicated to be rejected under 35 U.S.C. § 112, paragraph one, as allegedly not being enabled. As Claims 27-32 were previously canceled without prejudice, the present response will be directed at this rejection as applied to pending Claims 21-26.

(2) Claims 21-22 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Stevenson FK, *et al.*, (Meeting abstract, Gene Therapy of Cancer; 2nd European Conference, Sept. 7-8, 1995, London, A14, hereinafter "Stevenson").

(3) Claims 21-26 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious in light of Stevenson *et al.*, in view of Kwak, *et al.* (N. Eng. J. Med 1992 Oct; 327(17):1209-15, hereinafter "Kwak").

1. The Claims are Enabled

Claims 21-26 are rejected under 35 U.S.C. § 112, paragraph one, as allegedly not being enabled. The Examiner admits that the specification is enabling for a method of treating B-cell lymphoma comprising the administration of a multivalent anti-idiotypic *compound* comprising at least two heavy chain variable regions or two light chain variable regions of an immunoglobulin. (Office Action, page 2). However, the Examiner asserts that the specification does not provide enablement for a treatment comprising the administration of a multivalent *vaccine* comprising at least two heavy chain variable regions or two light chain variable regions of an immunoglobulin. Thus, the Examiner's rejection under 35 U.S.C. § 112, paragraph one is based on his assertion that a "vaccine" must be "capable of working as a preventative regime" (Office Action, page 3, last line).

The Examiner's interpretation of the term "vaccine" as used in the field of the present invention, cancer immunotherapy, is in error. As noted in the review by TRJ Evans cited by the Examiner (Office Action, page 3), "***[u]nlike* most vaccines for infectious agents, the**

goal of cancer vaccination is *therapeutic*," (TRJ Evans, Q J Med 1999; 92:299, column 1, second paragraph, emphasis added). Cancer vaccines are used to stimulate the immune system to "attack and reject **established** tumours" (emphasis added; Evans et al, at page 303, column 2), *i.e.*, they are used as a method for treating *existing* cancers, such as the Examiner admits is provided by the compositions of Claims 21-26 of the present application. Thus, the use of the term "vaccine" to describe the immunogenic compositions used in the methods of the present invention is wholly consistent with the meaning of this term as understood by those skilled in the art of cancer immunotherapy. The specification thus provides enablement for a treatment comprising the administration of a multivalent vaccine comprising at least two variable regions of an immunoglobulin derived from a B-cell lymphoma.

Nonetheless, in order to further Applicant's business interests and the prosecution of the present application in a manner consistent with Patent Business Goals, and not in acquiescence to the Examiner's arguments, and while reserving the right to prosecute the original (or similar) claims in the future, Applicant has amended Claims 21-23 to recite a "composition for active idiotype immunotherapy." The amendments to the claims made herein are not intended to narrow the scope of the claims within the meaning of *Festo*[1] or related cases. Support for the term "active idiotype immunotherapy" is found, *e.g.*, at the first sentence of Example 10, on page 88, where it is disclosed that active immunotherapy for B-cell lymphoma involves production of a vaccine comprising the immunoglobulin idiotype corresponding to an antibody on the surface of the B-cell tumor.

Applicant asserts that amended Claims 21-26 are enabled by the disclosure in accordance with 35 U.S.C. § 112, paragraph one, and respectfully requests that this rejection be removed.

2. Claims 21 and 22 are Not Anticipated

The Examiner alleges that Claims 21 and 22 are anticipated under 35 U.S.C. § 102(b) by Stevenson. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP 2131, citing *Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d. 628, 631, 2 USPQ2d 1051,*

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[1] *Festo Corp. v. Shokestu Kinzoku Kogyo Kabushiki Co.*, 122 S. Ct. 1831 (2002)

1053 (Fed. Cir. 1987). Stevenson does not set forth each and every element of Claims 21 and 22.

Claims 21 and 22 are drawn to a method of treating a B-cell lymphoma comprising administration a multivalent composition comprising at least two recombinant heavy chain variable regions of immunoglobulin molecules that differ by at least one idiotope.

The Stevenson reference does not describe methods of treatment using immunoglobulin compositions, either multivalent or otherwise. Rather, Stevenson relates to the replacing ***protein*** antigens such as immunoglobulins with ***DNA*** vaccines. The only mention of protein production by Stevenson is a brief statement that amplified products from a model murine lymphoma and from selected patients with lymphoma have been "assembled as single chain Fv sequences" and expressed *in vitro* in bacteria or mammalian cells. There is **no** information about the composition(s) of the assembled single chain Fv sequences, i.e., how many variable regions are encoded and whether they are light chain and/or heavy chain-encoding regions. There is **no** suggestion that the assembled scFV sequences encode at least two recombinant heavy chain variable regions of immunoglobulin molecules that differ by at least one idiotope, as recited in Claims 21 and 22. Furthermore, there is **no** suggestion that the proteins expressed from the constructs were used as a treatment. Rather, the only treatment suggested by Stevenson is vaccination via direct injection of naked DNA.

Stevenson does not teach or suggest methods of treating a B-cell lymphoma comprising administration of *any* protein, much less the claimed multivalent composition comprising at least two recombinant heavy chain variable regions of immunoglobulin molecules that differ by at least one idiotope. Therefore, Stevenson clearly does not set forth "each and every element" of *either* Claim 21 or Claim 22 and consequently cannot anticipate these claims. Applicant respectfully requests that this rejection be removed.

3. The Claims are Nonobvious

The Examiner alleges that Claims 21-26 are unpatentable under 35 U.S.C. § 103(a) over of Stevenson in view of Kwak. Applicant respectfully disagrees.

Prima facie obviousness requires: 1) a suggestion or motivation in the references or the knowledge generally available to combine or modify the reference teachings; 2) a reasonable expectation of success should the suggested combination or modification take

place; and 3) a teaching or suggestion of all the limitations of the claims. A showing of obviousness will fail if any one of these elements is not met. MPEP § 2143. Applicant submits that the combination of the Stevenson and Kwak references fails on all three elements.

As described above, Stevenson teaches treatment of B-cell lymphoma by vaccination via direct injection of naked DNA. Kwak teaches the treatment of B-cell lymphoma by administration of immunoglobulins isolated from a patient sample in combination with adjuvants and carrier proteins. Neither Stevenson nor Kwak teach or suggest methods of treating a B-cell lymphoma comprising administration of a recombinant protein composition, much less the claimed multivalent composition comprising at least two recombinant heavy chain variable regions of immunoglobulin molecules that differ by at least one idiotope.

In establishing *prima facie* obviousness, an examiner must make a showing of a teaching or motivation to combine prior art references. MPEP § 2143.01 . Here, the Examiner asserts that the present invention is obvious in light of Stevenson in view of Kwak. (Office Action, page 6). The Examiner asserts that one of ordinary skill would be motivated to combine the references to produce vaccines comprising the idiotypic determinants of scFVs allegedly taught by Stevenson with the use of adjuvants and carrier proteins taught by Kwak. However, the Examiner fails to address the fundamental difference between the DNA vaccine taught by Stevenson and the immunoglobulin proteins of Kwak. As detailed in the discussion above, Stevenson provides no teaching regarding the number and identity of the variable regions encoded by the scFv DNA vaccine. Furthermore, Stevenson provides no information on the nature of the idiotypic determinants when naked DNA is used in direct injection, so it cannot be asserted that these bear any similarity to the multivalent immunoglobulin compositions of Claims 21-26. Finally, the Examiner provides no indication of why one of ordinary skill would be motivated to make a combination between the DNA vaccines and the adjuvants and carrier proteins of Kwak, or why there should be any expectation of success at in making such a combination.

These reasons alone are sufficient to show that these references cannot be combined to create a case for prima facie obviousness of Claims 21-26. Still further, though, even if combined as the Examiner suggests, these references do not teach or suggest the all of the

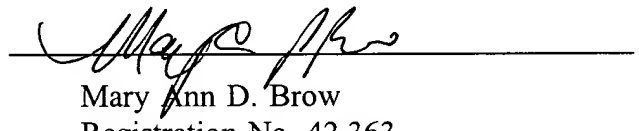
limitations of the claims, as required to show *prima facie* obviousness. Neither reference teaches or suggests multivalent compositions comprising at least two recombinant heavy chain variable regions of immunoglobulin molecules that differ by at least one idiotope, or methods of treating a B-cell lymphoma comprising administration of such protein compositions. The improper combination of these references, even if made, does not cure this deficiency.

For the reasons set forth above, Claims 21-26 are not obvious under 35 U.S.C. § 103(a) in light of Stevenson in view of Kwak, and Applicant respectfully requests that this rejection be removed.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all grounds for rejection should be removed and Applicant's claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: October 17, 2003



Mary Ann D. Brow
Registration No. 42,363
MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105